CLAIMS

1. A crystal of ACE protein.

2. A crystal according to claim 1 wherein the ACE protein is underglycosylated.

3. A crystal according to claim 2 wherein the ACE protein is underglycosylated by removing one or more glycosylation sites and/or one or more partially glycosylated sites.

4. A crystal according to claim 3 wherein the underglycosylated ACE protein comprises a mutation at amino acid 337 or amino acid 90, 109, 155, 337 and 586 of SEQ ID No 2.

5. A crystal according to any one of the preceding claims comprising atoms arranged in a spatial relationship represented by at least a portion of the structure co-ordinates of Table A or Table B.

6. A crystal according to any one of the preceding claims wherein the crystal belongs to the space group $P2_12_12_1$.

7. A crystal according to any one of the preceding claims having unit cell dimensions of: a= 56.47 Å, b=84.90 Å, c=133.99 Å.

8. A crystal according to any one of the preceding claims wherein the crystal is a crystal of human ACE protein.

9. A crystal according to any one of the preceding claims wherein the crystal further comprises an entity bound to the ACE protein or a portion thereof.

10. A crystal according to claim 9 wherein the entity is bound to the ACE protein or a portion thereof by contacting one or more residues of the ACE protein selected from: His384, Ala385, Lys542, Tyr551, Tyr554, Glu415 and His544.

11. A crystal according to claim 9 or claim 10 wherein the entity modulates the activity of ACE.

12. A crystal according to claim 11 wherein the entity is an inhibitor of ACE.

13. A crystal according to claim 12 wherein the inhibitor of ACE is lisinopril or a derivative thereof.

14. A crystal according to claim 13 comprising atoms arranged in a spatial relationship represented by at least a portion of the structure co-ordinates of Table B.

15. A method of preparing a crystal of ACE protein comprising the steps of:

(a) culturing host cells comprising an underglycosylated ACE protein;
(b) purifying the underglycosylated ACE protein; and
(c) crystallising the underglycosylated ACE protein.

16. A method according to claim 15 wherein the ACE protein is underglycosylated by removing one or more glycosylation sites and/or one or more partially glycosylated sites.

17. A method according to claim 15 or claim 16 wherein the underglycosylated ACE protein comprises a mutation at amino acid 337 of SEQ ID No 2 or amino acids 90, 109, 155, 337 and 586 of SEQ ID No 2.

18. A method according to any of claims 15 to 17 wherein the ACE protein is crystallised using about 10 mM HEPES and about 0.1% PMSF with an equal volume of a reservoir solution containing about 15 % PEG 4000, about 50 mM $CH_3COONa.3H_2O$ pH 4.7 and about 10 μM $ZnSO_4.7H_2O$.

19. A method according to any of claims 15 to 18 wherein the crystal that is prepared has a structure defined by at least a portion of the structure co-ordinates of Table A.

20. A method according to any of claims 15 to 19 wherein the crystal belongs to the space group $P2_12_12_1$.

21. A method according to any of claims 15 to 20 wherein the crystal has the unit cell dimensions: a= 56.47 Å, b=84.90 Å and c=133.99 Å.

22. A method according to any of claims 15 to 21 wherein the ACE protein is human ACE protein.

23. A method according to any of claims 15 to 22 wherein the ACE protein is crystallised in the presence of an entity.

24. A method according to claim 23 wherein the entity is a modulator of ACE.

25. A method according to claim 24 wherein the entity is an inhibitor of ACE.

26. A method according to claim 25 wherein the inhibitor of ACE is lisinopril or a derivative thereof.

27. A method according to claim 26 wherein the crystal that is prepared has a structure defined by at least a portion of the structure co-ordinates of Table B.

28. A method of screening for a modulator of ACE wherein the method comprises the use of a crystal according to any of claims 1-14.

29. A method according to claim 28 comprising the steps of:

(a) providing at least a portion of the structure co-ordinates of Table A or Table B;

(b) employing at least a portion of the structure co-ordinates of Table A or Table B to design or select or synthesise a putative modulator of ACE;

(c) contacting the putative modulator of ACE with ACE or a mutant, variant, homologue, derivative or fragment thereof in the presence of a substrate; and

(d) screening the putative modulator of ACE in an assay for the potential to modulate ACE.

30. A method according to claim 29 wherein at least a portion of the structure co-ordinates of Table A or Table B and/or the putative modulator of ACE and/or the substrate are provided on a machine-readable data storage medium comprising a data storage material encoded with machine readable data.

31. A method according to claim 29 or claim 30 wherein the putative ACE modulator is from a library of compounds.

32. A method according claim 29 or claim 30 wherein the putative ACE modulator is selected from a database.

33. A method according to claim 29 or claim 30 wherein the putative ACE modulator is designed *de novo*.

34. A method according to claim 29 or claim 30 wherein the putative ACE modulator is designed from a known ACE modulator.

35. A method according to claim 29 or claim 30 wherein the design or selection of the putative ACE modulator is performed in conjunction with computer modelling.

36. A method according to any of claims 28 to 35 wherein the ACE modulator is useful in the prevention and/or treatment of an ACE related disorder.

37. A method according to claim 36 wherein the ACE related disorder is hypertension.

38. A process comprising the steps of:

(a) performing the method according to any of claims 28 to 36;

(b) identifying one or more modulators of ACE; and

(c) preparing a quantity of those one or more ACE modulators.

39. A process comprising the steps of:

(a) performing the method according to any of claims 28 to 36;

(b) identifying one or more ACE modulators; and

(c) preparing a pharmaceutical composition comprising those one or more identified ACE modulators.

40. A process comprising the steps of:

(a) performing the method according to any of claims 28 to 36;

(b) identifying one or more ACE modulators;

(c) modifying those one or more ACE modulators; and

(d) optionally preparing a pharmaceutical composition comprising those one or more ACE modulators.

41. A method of obtaining structural information about a molecule or a molecular complex of unknown structure by using at least a portion of the structure co-ordinates of ACE, comprising the steps of:

(a) generating X-ray diffraction data from a crystallised molecule or molecular complex;

(b) applying at least a portion of the structure co-ordinates of ACE to said X-ray diffraction pattern to generate a three dimensional electron density map of at least a portion of the molecule or molecular complex; and

(c) using all or a portion of the structure co-ordinates of ACE to generate homology models of ACE.

42. An ACE modulator identified by the method of any one of claims 28 to 36.

43. An ACE modulator according to claim 42 wherein the ACE modulator inhibits ACE.

44. A pharmaceutical composition comprising an ACE modulator according to claim 42 or claim 43 and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant or any combination thereof.

45. A method of preventing and/or treating an an ACE related disorder comprising administering a modulator of ACE according to claim 42 or claim 43 and/or a pharmaceutical according to claim 44 wherein said modulator of ACE or said pharmaceutical is capable of causing a beneficial preventative and/or therapeutic effect.

46. A computer for producing a three-dimensional representation of ACE wherein said computer comprises:

(a) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises the structure co-ordinates of ACE;

(b) a working memory for storing instructions for processing said computer-readable data;

(c) a central-processing unit coupled to said working memory and to said computer-

readable data storage medium for processing said computer-machine readable data into said three-dimensional representation; and

(d) a display coupled to said central-processing unit for displaying said three-dimensional representation.

47. A machine-readable data storage medium comprising a data storage material encoded with machine readable data, wherein the data is defined by at least a portion of the structure co-ordinates of ACE in Table A or Table B.

48. Use of an ACE crystal in the preparation of a medicament to prevent and/or treat an ACE related disorder.

49. Use according to claim 48 wherein the ACE related disorder is hypertension.

50. Use of at least a portion of the structure co-ordinates of Table A or Table B to screen for modulators of ACE.

51. Use of at least a portion of the structure co-ordinates of Table A or Table B to solve the structure of the crystalline form of any other protein with significant amino acid sequence homology to any functional domain of ACE.

52. Use of at least a portion of the structure co-ordinates of Table A or Table B in molecular design techniques to design, select and synthesise modulators of ACE.

53. Use of at least a portion of the structure co-ordinates of Table A or Table B in the development of compounds that can isomerise to reaction intermediates in the chemical reaction of a substrate or other compound that binds to ACE.

54. Use of at least a portion of the structure co-ordinates of Table A or Table B to screen small molecule databases for chemical entities or compounds that modulate ACE.

55. Use of at least a portion of the structure co-ordinates of Table A or Table B to solve the structure of the crystalline form of any other protein with significant amino acid sequence homology to any functional domain of ACE.

56. Use according to claim 55 wherein the structure of the crystalline form of any other protein with significant amino acid sequence homology to any functional domain of ACE is solved using molecular replacement.

57. pLEN- tACEΔ36g(1, 2, 3, 4).

58. pLEN- tACEΔ36g(1,3).